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CAROLINE M. NASH
NASH & TITUS
3415 BROOKSVILLE ROAD
SUITE 1000
BROOKSVILLE, MD 20833

EXAMINER	
SISSON, BRADLEY L	
ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/444,095	IBRAHIM, SOFI M.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/26/03 & 12/4/ 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-35,38,39,63 and 65-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-35,38,39,63 and 65-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Specification

1. The specification is objected to as documents have been improperly incorporated by reference. In particular, the specification states that the cited documents "are herein incorporated by reference." Such omnibus language fails to specify what specific information applicant seeks to incorporate by reference and similarly fails to teach with detailed particularity just where that specific information is to be found in each of the cited documents. As set forth in *Advanced Display Systems Inc. v. Kent State University* (Fed. Cir. 2000) 54 USPQ2d at 1679:

> Incorporation by reference provides a method for integrating material from various documents into a host document--a patent or printed publication in an anticipation determination--by citing such material in a manner that makes it clear that the material is effectively part of the host document as if it were explicitly contained therein. *See General Elec. Co. v. Brenner*, 407 F.2d 1258, 1261-62, 159 USQP 335, 337 (D.C. Cir. 1968); *In re Lund*, 376 F.2d 982, 989, 153 USPQ 625, 631 (CCPA 1967). **To incorporate material by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents.** *See In re Seversky*, 474 F.2d 671, 674, 177 USPQ 144, 146 (CCPA 1973) (providing that incorporation by reference requires a statement "clearly identifying the subject matter which is incorporated and where it is to be found"); *In re Saunders*, 444 F.2d 599, 602-02, 170 USPQ 213, 216-17 (CPA 1971) (reasoning that a rejection or anticipation is appropriate only if one reference "expressly incorporates a particular part" of another reference); *National Latex Prods. Co. v. Sun Rubber Co.*, 274 F.2d 224, 230, 123 USPQ 279, 283 (6th Cir. 1959) (requiring a specific reference to material in an earlier application in order to have that material considered a part of a later application); *cf. Lund*, 376 F.2d at 989, 13 USPQ at 631 (holding that **a one sentence reference to an abandoned application is not sufficient to incorporate from the abandoned application into a new application**). (Emphasis added.)

Accordingly, the cited documents are not considered to have been properly incorporated by reference and as such, have not been considered with any effect towards their fulfilling, either in

part or in whole, the enablement, written description, or best mode requirements of 35 USC 112, first paragraph.

Response to argument

2. At page 7 of the response of 26 June 2003, hereinafter the response, applicant states:

> The Examiner's new assertion that the subject incorporated by reference is improper is without merit. The first sentence of the first full paragraph on page 8 of the specification recites:
>
> *The capture of nucleic acids, proteins or cells either non-specifically or by affinity binding onto solid phase supports as well as colorimetric, luminiscent, fluorescent and electrochemical detection are well known in the art as described in the following and other references, of which these are incorporated by reference:*
>
> This statement clearly indicates why the numerous publications are incorporated by reference, i.e. to show how to capture nucleic acids, proteins or cells..... Most of the references indicate the specific page numbers as well as volume numbers and dates so the requirement of showing where to find the incorporated subject matter has been met in the present specification.

Agreement is reached in that there are indeed numerous articles that, through the use of but one omnibus sentence, applicant seeks to incorporate by reference. For convenience, pages 8 and 9 of the specification, in pertinent part, are reproduced below.

other references, of which these are herein incorporated by reference: Ausubel F., Brent R., Kingston R.E., Moore D.D., Seidman J.G., Smith J.A., Struhl K., (1987). Current Protocols in Molecular Biology. Greene Publishing Associates and Wiley-Intersciences. John Wiley & Sons, New York, Chichester, Brisbane, Toronto, Singapore.; Sambrook J., Fritsch EF, Maniatis J. (1989). Molecular cloning: A laboratory manual. 2nd edition, Cold Spring Harbor laboratory Press, Cold Spring Harbor, New York.; Hornes E., Korsnes L. (1990). Magnetic DNA hybridization properties of oligonucleotide probes attached to superparamagnetic beads and their use in the isolation of poly(A) mRNA from eukaryotic cells. Genet. Anal. Tech. Appl. 7:145-150.; Jakobsen K.S., Haugen M., Saeboe-Larsen S., Hollung K., Espelund M., Hornes E. (1994). Direct mRNA isolation using magnetic Oligo(dT) beads: A protocol for all types oc cell cultures, animal and plant tissues. In: Advances in Biomagnetic Separation, (Ed. Uhlen M., Hornes E., Olsvik O) Eaton Publishing pp.61-71.; Rodriguez I.R., Chader G.J. (1992). A novel method for the isolation of tissue specific genes. Nucleic Acids Res. 18:4833-4842.; Schussler P., Gohr L.G., Sommer G., Kunz W., Grevelding C.G. (1995). Combined isolation of nucleic acids and proteins from small amounts of tissue. Trends Genet. 11:378-379.; Beattie K.L., Fowler R.F. (1991). Solid-phase gene assembly. Nature 352:548-552.; Rudi K., Kroken M., Dahlberg O.J., Deggerdal A., Jakobsen K.S., Larsen F. (1997).

Rapid, universal method to isolate PCR-ready DNA using magnetic beads. BioTechniques 22:506-511.; Collin-Osdoby P., Oursler M.J., Webber D., Osdoby P. (1991). Osteoclast-specific monoclonal antibodies coupled to magnetic beads provide a rapid and efficient method of purifying avian osteoclasts. J. Bone Mine. Res. 6:1353-1365.; Cudjoe K.S., Krona R., Olsen E. (1994). IMS: A new selective enrichment technique for the detection of salmonella in foods. Int. J. Food Microbiol. 23:159-165.; Elgar G.S., Brenner S. (1992). A novel method for isolation of large insert DNA from recombinant lambda DNA. Nucleic Acids Res. 20:4667.; Gabrielsen O.S., Huet J. (1993). Magnetic DNA affinity purification of yeast transcription factor. Meth. Enzymol. 218:508-525.; Hames B.D., Higgins S.J. (1985). Nucleic acid hybridization: A practical approach. IRL Press, Oxford, England.; Hawkins R.E., Russell S.J., Winter G. (1992). Selection of phage antibodies by binding affinity. Mimicking affinity maturation. J. Mol. Biol. 226:889-896.; Boom, R., Sol, C.J., Salimans, M.M., Jansen, C.L., Wertheim-van Dillen, P.M., and van der Noordaa, J. (1990). Rapid and simple method for purification of nucleic acids. J. Clin. Microbiol., 28(3):495-503.; Lundeberg J., Larsen F. (1995). Solid-phase technology:magnetic beads to improve nucleic acid detection and analysis. Biotechnology Annual Review 1:373-401.; Millar D.S., Withey S.J., Tizard M.L.V., Ford J.G., Hermon-Taylor J. (1995). Solid-phase hybridization capture of low abundance target DNA sequences: application to the polymerase chain reaction detection of Mycobacterium paratuberculosis and Mycobacterium avium susp. Silvaticum. Anal. Biochem. 226:325-330.; Vlieger A.M., Medenblik A.M.J.C., Van Gijlswijk R.P.M., Tanke H.J., Van der Ploeg M., Gratama J.W., Raap A.K. (1992). Quantitation of polymerase chain reaction products by hybridization-based assays with fluorescent, colorimetric or chemiluminescent detection. Anal. Biochem. 205:1-7.

While applicant has provided a bibliographic cite for the documents for some of the documents, such citations, when provided, do not teach with detailed particularity just where within each of the documents the specific information is to be found. Accordingly, and in the absence of convincing evidence to the contrary, the objection of the specification hs been maintained.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 31-35, 38, 39, 63, and 65-70 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

> To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

5. For convenience, claims 31, 63, and 70, the only independent claims, are reproduced below.

31. (previously amended) A method of DNA or RNA purification comprising:

placing a DNA or RNA containing sample in a first reservoir tube with a solution to effect release of DNA or RNA from cells in said sample;

inserting a wand into said first reservoir tube, wherein said wand comprises a cap, a sample collection assembly and an elongated shaft connecting said cap to said sample collection assembly, said sample collection assembly having microstructures for increasing the surface area of the sample collection assembly;

securely and sealingly closing said first reservoir tube with said cap of said wand with said shaft and said sample collection assembly inside said first reservoir tube;

agitating said first reservoir tube to mix said sample with said solution under conditions for releasing said DNA or RNA from cells in said sample and non-specifically binding said DNA or RNA to said microstructures of said sample collection assembly, thereby non-specifically binding said DNA or said RNA to said microstructures of said sample collection assembly;

removing said wand from said first reservoir tube and inserting said wand into a second reservoir tube, said second reservoir tube containing a wash buffer;

securely and sealingly closing said second reservoir tube with said cap of said wand with said shaft and said sample collection assembly inside said second reservoir tube;

agitating said second reservoir tube to mix said sample with said wash buffer under conditions to retain only said DNA or said RNA on said microstructures;

removing said wand from said second reservoir tube and inserting said wand into a third reservoir tube, said third reservoir tube containing an elution buffer, wherein said elution buffer causes release of said nucleic acids from said microstructures;

incubating said third reservoir tube; and

recovering purified DNA or RNA from said third reservoir tube.

63. (previously amended) A method of purifying specific DNA or RNA comprising:

placing a purified DNA or RNA sample in a first reservoir tube under conditions to denature double stranded DNA or render RNA suitable for binding;

inserting a wand into said first reservoir tube, wherein said wand comprises a cap, a sample collection assembly and an elongated shaft connecting said cap to said sample collection assembly, said sample collection assembly having microstructures for increasing the surface area of the sample collection assembly, and said microstructures of said sample collection assembly are coated with a coating comprising sequence specific oligonucleotide probe, peptide nucleic acid probe through a linker arm, or biotin-streptavidin bond to capture specific target DNA or RNA;

securely and sealingly closing said first reservoir tube with said cap of said wand with said shaft and said sample collection assembly inside said first reservoir tube, and incubating said DNA or said RNA of the sample in the sample collection assembly under conditions whereby stable, specific hybridization structures are formed, thereby binding said specific DNA or said specific RNA to said coating on said microstructures of said sample collection assembly;

removing said wand from said first reservoir tube and inserting said wand into a second reservoir tube, said second reservoir tube containing a wash buffer;

securely and sealingly closing said second reservoir tube with said cap of said wand with said shaft and said sample collection assembly inside said second reservoir tube;

agitating said second reservoir tube to mix said sample with said wash buffer under conditions to retain only said DNA or said RNA on said microstructures;

removing said wand from said second reservoir tube and inserting said wand into a third reservoir tube, said third reservoir tube containing an alkaline elution buffer to effect release of said DNA or said RNA;

incubating said third reservoir tube;

removing said sample collection assembly from said third reservoir tube;

adding neutralization buffer to said third reservoir tube to stabilize said DNA or said RNA; and

recovering said specific DNA or RNA from said third reservoir tube.

70. (previously added) A method of purifying specific DNA or RNA comprising:

placing a purified DNA or RNA sample in a first reservoir tube under conditions to denature double stranded DNA or render RNA suitable for binding;

inserting a wand into said first reservoir tube, wherein said wand comprises a cap, a sample collection assembly and an elongated shaft connecting said cap to said sample collection assembly, said sample collection assembly having microstructures for increasing the surface area of the sample collection assembly, and said microstructures of said sample collection assembly are coated with a coating comprising sequence specific oligonucleotide probe, peptide nucleic acid probe through a linker arm, or biotin-streptavidin bond to capture specific target DNA or RNA;

removing said wand from said first reservoir tube and inserting said wand into a second reservoir tube, said second reservoir tube containing a wash buffer;

securely and sealingly closing said second reservoir tube with said cap of said wand with said shaft and said sample collection assembly inside said second reservoir tube;

agitating said second reservoir tube to mix said sample with said wash buffer under conditions to retain only said DNA or said RNA on said microstructures;

removing said wand from said second reservoir tube and inserting said wand into a third reservoir tube;

heating said third reservoir tube under conditions to effect release of said DNA or said RNA from said microstructures;

removing said sample collection assembly from said third reservoir tube; and

recovering said specific DNA or RNA from said third reservoir tube.

6. For purposes of examination, the claimed methods have been interpreted as encompassing the isolation of any DNA or RNA; wherein said DNA can be of any length, e.g., oligonucleotides to intact chromosomes. Said RNA has been interpreted as encompassing any

and all RNAs, which include mRNA, tRNA, rRNA, mitochondrial RNA. Said method of isolating DNA and RNA has been interpreted as fairly encompassing the isolation of any and all quantities of said DNA and/or RNA as found in any source, including intact tissue from plants, rock, crude oil, bone, aerosol, etc., and where the DNA or RNA can be of virtually quantity.

7. As noted above under the objection to the specification, documents cited therein have not been properly incorporated by reference and as such, the disclosure of reaction conditions and starting materials as found in said cited documents are not available in satisfying the written description requirement of the now claimed method.

8. A review of the specification finds four examples:

a. Example 1, pages 11-12, "Nucleic Acid Purification,"

b. Example 2, page 12, "Nucleic Acid Detection;"

c. Example 3, page 13, "Antigen Capture and Detection,"

d. Example 4, pages 13-14, "Antibody Capture and Detection."

9. Of the four examples, only Example 1 is considered to be relevant to the claimed and elected invention. For convenience, Example 1 is reproduced below.

Nucleic Acid Purification

In a typical nucleic acids purification, mix 10-100 µl of sample with 100 µl of lysis/denaturing buffer in a 1.5 ml reservoir tube. Insert the shaft and sample capture assembly of the wand into the reservoir tube and close the reservoir tube with the cap. Vortex the reservoir tube for about 1 minute. Incubate the reservoir tube at 37°C for about 5 minutes. Remove the wand, and insert the wand into a fresh reservoir tube containing 1000 µl of wash buffer. Vortex the reservoir tube for about 1 minute. Remove the wand and insert it into a fresh reservoir tube containing 100 µl of elution buffer. Heat the reservoir tube to abut 65°C for about 5 minutes. The DNA or RNA is now purified and ready for further analysis or processing.

10. While the specification does clearly describe using cross-etched lanes that range in depth from 0.001 to 2 mm (page 7), microparticles that range in size from 1 to 500 µm in diameter (page 7), and a sample volume that ranges from 10 to 100 µl, the specification, including the above example does not identify/teach/describe:

- The source of the sample,
- The composition of the lysis/denaturing buffer or wash buffer,
- Any description of limitless cross-etched lanes (claims 33), dimples (claim 33), pillars (claim 33), pores (claim 33),
- The use of silicon oxide or aluminum oxide,
- The use of a neutralization buffer so to stabilize said DNA or said RNA prior to recovery (claim 63); or
- The heating of the DNA or NRA in the third tube without the addition of an elution buffer (claim 70).

11. The specification does not provide an adequate written description of how, for example, mitochondrial DNA or RNA is to be isolated from any sample. The sensitivity of RNA to degradation is well known. The specification, however, does not provide an adequate description of how this art-recognized problem would be overcome as it relates to the use of the recited wand.

12. As presently worded, the method of claims 63 and 70 fairly encompass the use of any probe that would bind to any nucleic acid of interest. Such language fairly encompasses a method of detecting any sequence of interest, including, but not limited to, any disease state in any and all life forms, genes related to weight control, intelligence, predisposition to any condition, known and unknown, as well as the simultaneous detection of any and all nucleic acids, including point mutations of all genes in all life forms, in a simultaneous manner. A review of the disclosure fails to find an adequate written description of any "probe," much less a probe that is bound through any linker arm or biotin-streptavidin bond to any microstructure.

13. It is noted that page 8, first paragraph, states in pertinent part:

> conductivity. The sample collection assembly can also be coated with singular or dendritic oligonucleotide probes, peptide probes or cell receptors to capture specific target molecules. The use of dendritic probes in conjunction with the sample collection assembly described herein can further significantly increase the capture surface area and significantly enhance analytical and clinical sensitivity.

14. The specification has not been found to provide an adequate written description of the broad genus of probes that would be required to practice the claimed invention. While one may assert that alternative embodiments would be obvious, obviousness does take the place of an adequate written description of the invention such that the specification reasonably suggests that

applicant was in possession of the full scope of the claimed invention. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

Accordingly, and in the absence of convincing evidence to the contrary, applicant is urged to consider narrowing the claims to those embodiments adequately supported by the original disclosure.

Response to arguments

15. Starting at page 6, last paragraph, bridging to page 9, applicant presents a traversal of the rejection of claims under 35 USC 112, first paragraph. It is noted that the traversal addresses issues of enablement, asserting what the level of skill in the art was, and what certain prior art publications disclose. Such arguments, however, have not been found persuasive in overcoming the rejection of claims under 35 USC 112, first paragraph, as failing to comply with the written description requirement. As noted above, the written description component of 35 USC 112, first paragraph, is not satisfied by showings of the level of skill in the art or by showing of obviousness. Rather, "[t]o satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing." *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428. Such full and detailed description of every element of the claimed invention is not found

in the instant specification. Therefore, and in the absence of convincing evidence to the contrary, the rejection is maintained.

16. Claims 31-35, 38, 39, 63, and 65-70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the isolation of DNA where a wash buffer of 1.0 M NaCl, 50 mM MOPS, 15% ethanol, pH 7.0 is used along with an elution buffer of 1.25 M NaCl, 50 mM Tris HCl, 15% ethanol, pH 8.5, where the sample ranges in size from 10-1000 µl and the elution step further comprises heating the sample to 65 C, does not reasonably provide enablement for the use of alternative wash, elution buffers, sample sizes, and reaction conditions.

17. As set forth in *Enzo Biochem Inc., v. Calgene, Inc.* (CAFC, 1999) 52 USPQ2d at 1135, bridging to 1136:

> To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).... We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, *e.g.*, *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In *In re Wands*, we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co.*,

> *Ltd.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors "are illustrative, not mandatory. What is relevant depends on the facts.").

18. It is well settled that one cannot enable that which they do not yet posses. And as shown above, the description found in the instant describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Further, documents cited within the disclosure, while available as background information, are not properly incorporated by reference and therefore cannot be relied upon for satisfying the enablement, written description, or best mode requirements of 35 USC 112, first paragraph. As set forth in *Enzo Biochem Inc., v. Calgene, Inc.* (CAFC) 52 USPQ2d at 1135, bridging to 1136:

> To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).... We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, *e.g.*, *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In *In re Wands*, we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors "are illustrative, not mandatory. What is relevant depends on the facts.").

19. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. As presently worded, the claimed methods encompass the use of virtually any lysis, wash and elution buffer and sample size. Of the four prophetic examples provided, only Example 1, pages 11-12, is related to the claimed invention. The prophetic example asserts that RNA could be isolated by the disclosed method; however, the presence of ribonucleases in a sample would readily destroy any RNA present. The method does not disclose the use of any agent that would prevent such degradation. Additionally, none of the claims recite any step that would allow for the preservation of RNA while in the presence of degradative enzymes such as ribonucleases. In view of such art-recognized difficulties, and finding no claimed limitation that would allow for the isolation of RNA while being subjected to a degradative environment, the skilled artisan would have to develop alternative, and non-disclosed methods. Such alternative methods would require a level of experimentation beyond the routine experimentation that is allowed for under 35 USC 112, first paragraph. The specification also does not enable the use of probes to capture specific nucleic acid sequences as no starting materials (e.g., specific probes) are provided, nor does the specification set forth the reaction conditions under which the method of claims 63, 65, 66, 68, 69, and 70 is to be practiced.

20. For the above reasons, and in the absence of convincing evidence to the contrary, applicant is urged to consider narrowing the claims to those embodiments adequately supported by the disclosure.

Response to argument

21. Page 7, first paragraph, of the response of 26 June 2003, applicant asserts:

> paragraph). Applicants provided the pages of Boom, et al that clearly identified the subject matter which is incorporated by reference (pages 495-503 of Boom et al. as indicated at page 9, line 15). Boom et al. makes clear that one of ordinary skill in the art

22. For convenience, page 9, lines 13-15 of the specification are reproduced below.

> maturation. J. Mol. Biol. 226:889-896.; Boom, R., Sol, C.J., Salimans, M.M., Jansen, C.L., Wertheim-van Dillen, P.M., and van der Noordaa, J. (1990). Rapid and simple method for purification of nucleic acids. J. Clin. Microbiol., 28(3):495-503.; Lundeberg J., Larsen F. (1995). Solid-phase technology:magnetic beads to improve nucleic acid

23. As an initial matter, it is noted that applicant has simply provided a bibliographic citation for the document; infra.

JOURNAL OF CLINICAL MICROBIOLOGY, Mar. 1990, p. 495–503
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Rapid and Simple Method for Purification of Nucleic Acids

R. BOOM,[1]* C. J. A. SOL,[2] M. M. M. SALIMANS,[2] C. L. JANSEN,[1] P. M. E. WERTHEIM-VAN DILLEN,[2] AND J. VAN DER NOORDAA[1]

Department of Virology, Academic Medical Center, Meibergdreef 15, 1105 AZ Amsterdam,[1] and Department of Virology, University Hospital Leiden, 2333 AA Leiden,[2] The Netherlands

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As noted above, a bibliographic citation is not considered to be a proper attempt to incorporate a document by reference for applicant has not identified with the required "detailed particularity" where the specific information is to be found within the cited document. While applicant at page 7 of the response now sates that Boom et al. is to be relied upon as rendering the claimed the type of wash buffer, type of elution buffer, amount of sample and conditions necessary to practice the invention, such statements of purpose of incorporation are not to be found in he original specification. Furthermore, a review of the document finds that page 503, which

applicant asserts discloses subject matter that is incorporated by reference, is simply a portion of the bibliographic index for the paper; *infra*.

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of nucleic acids. Methods Enzymol. 128:120–129.
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14. Kwok, S., and R. Higuchi. 1989. Avoiding false positives with PCR. Nature (London) 339:237–238.
15. Maniatis, T., E. F. Fritsch, and J. Sambrook. 1982. Molecular cloning: a laboratory manual, p. 194–197. Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.
16. Marko, M. A., R. Chipperfield, and H. C. Birnboim. 1982. A procedure for the large scale isolation of highly purified plasmid DNA using alkaline extraction and binding to glass powder. Anal. Biochem. 121:382–387.
17. Miller, R. H., S. Kaneko, C. T. Chung, R. Girones, and R. H. Purcell. 1989. Compact organization of the hepatitis B virus genome. Hepatology 9:322–323.
18. Norval, M., and R. W. Bingham. 1987. Advances in the use of nucleic acid probes in diagnosis of viral disease of man. Arch. Virol. 97:153–165.
19. Raptis, L., and H. A. Menard. 1980. Quantitation and characterization of plasma DNA in normals and patients with systemic lupus erythematosis. J. Clin. Invest. 66:1391–1399.
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25. Thompson, J., and D. Gillespie. 1987. Molecular hybridization with RNA probes in concentrated solutions of guanidine thiocyanate. Anal. Biochem. 163:281–291.
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28. von Hippel, P. H., and K. Y. Wong. 1964. Neutral salts: the generality of their effects on the stability of macromolecular conformations. Science 145:577–580.
29. Yang, R. C. A., J. Lis, and R. Wu. 1979. Elution of DNA from agarose gels after electrophoresis. Methods Enzymol. 65:176–182.

Accordingly, the cited pages that applicant wishes to incorporate by reference do not disclose the information that applicant now asserts is to be brought in via an incorporation by reference.

24. At page 8 of the response of 26 June 2003 applicant asserts "many tests according to the claimed method [has been performed] and RNA is not destroyed." Applicant also directs attention to prior art documents, and asserts that reagents such as guanidinium isothiocyanate (GITC) could be used.

25. The above argument has been fully considered and has not been found persuasive. As an initial matter, limitations found in applicant's arguments and/or in the specification are not read into the claims. Rather, the claims are read as broadly as is reasonably possible. Accordingly, the claims fairly encompass using virtually any set of conditions. Assuming *arguendo*, that

GITC could be used, the specification is silent as to its use. While documents have been cited, they again cannot be relied upon for fulfilling enablement, written description, or best mode requirements of 35 USC 112, first paragraph. Further, the aspect of isolating RNA from any source is not disclosed, yet disclosure of such methodology is critical to practicing the claimed invention. (Claim 31 states in the preamble that it is directed to "a method of DNA or RNA purification."

26. To the extent that chaotropic agents (e.g., GITC) could be used to practice the claimed invention as it elates to isolation of RNA, attention is directed to US Patent Application Publication 2003/0204077 A1, where at paragraph 7 states:

> [0007] The presence of chlorophyl and increased amounts of polysaccharides in plants provides additional problems for RNA isolation from such samples. In particular, the conventional use of chaotropic agents results in co-isolation of polysaccharides with the purified RNA. As plant cells have higher concentrations of polysaccharides, this problem is exacerbated by using known RNA isolation methods. (Emphasis added)

Accordingly, the specification does not teach how these art-recognized issues are to be overcome as it relates to the practice of the full scope of the invention.

In view of the breadth of scope clamed, the limited guidance provided, the unpredictable nature of the art to which the claimed invention is directed, and in the absence of convincing evidence to the contrary, the claims remain rejected under 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 103

27. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

28. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

29. Claims 31-35, 38, 39, 63, and 65-70 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,514,785 (Van ness et al.) in view of Boom et al., JP 7-308184 A and US Patent 5,637,687 (Wiggins).

30. Claims 31-35, 38, 39, 63, and 65-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Ness et al., (US Patent 5,514,785) in view of Boom et al., JP 7-308184 A and Wiggins (US Patent 5,637,687).

31. Van Ness et al., column 2, last two paragraphs, disclose the use of dipsticks that comprise beads and that nucleic acid are bound to the support. Column 8 teaches use of the beads in hybridization assays

32. Van Ness et al., do not disclose binding of nucleic acids to a silica oxide support, elution of captured nucleic acids, or use of a cap/wand/tube arrangement.

33. Boom et al., disclose that the binding of DNA to silica particles (applicant's silica oxide) is well known in the art. Boom et al., also disclose lysis, binding, and washing steps.

34. Boom et al., do not disclose use of a device that comprises a cap being integral to a wand and that when the wand is placed in a tube, it a sealing closure is affected.

35. JP 7-308184 discloses a wand that is integral to a cap lid and that when brought into closing proximity, a seal is established. The wand can be used for collection of biological samples that are in turn subjected to PCR.

36. Wiggins, column 4, bridging to column 5, disclose eluting captured nucleic acids from solid support that can comprise beads.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Van Ness et al., whereby the dipstick was substituted with the wand/cap/tube of JP 7-308184 such that biological samples could be collected and processed, and the nucleic acid material immobilized on the microstructures as disclosed by Van Ness et al., and Boom et al. would be eluted as disclosed by Wiggins. In view of the detailed guidance provided, the skilled artisan would have been both motivated and would have had a reasonable expectation of success. While the prior art clearly teaches performing lysis, washing and elution of nucleic acids, the selection of the number and duration of lysis, binding and elution steps and associated tubes is considered to be a matter of routine optimization. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

> Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In re Dreyfus, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52; In re Waite et al., 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In re Swenson et al., 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; In re Scherl, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility

> over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In re Sola, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; In re Normann et al., 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; In re Irmscher, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Swain et al., 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; Minnesota Mining and Mfg. Co. v. Coe, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; Allen et al. v. Coe, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

37. For the above reasons, and in the absence of convincing evidence to the contrary, claims 31-35, 38, 39, 63, and 65-70 remain rejected under 35 U.S.C. 103(a).

Response to arguments

38. Agreement is reached where at page 10 of the response of 26 June 2003 applicant asserts that the claimed invention has not been disclosed the cited references. It is noted that the claims have been rejected over the combined teachings of several pieces of prior art, and not under 35 USC 102, which deals with anticipation.

39. From page 10, bridging to page 11, applicant presents a rebuttal of each of the pieces of prior art. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

40. At page 10 of the response applicant asserts that a point of novelty resides in the aspect that Van Ness does not teach using a porous support or binding nucleic acids to a silica oxide support. This argument has not been found persuasive, as applicant is arguing limitations not present in the claims. Claims 31, 32, 35, 38, 39, 63, and 65-70 do not require the use of a porous support. Although the claims are interpreted in light of the specification, limitations from the

specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

41. While claims 33 and 34 do recite use of a porous support, such is optional, as other, non-porous microstructures can be used. It is further noted that claims 31-35, 38, 63, and 65-70 do not require the use of silica oxide. Yet, Van Ness, column 2, does teach explicitly of having beads on a dipstick wherein the beads comprise a probe that can be used to purify DNA or RNA from a solution.

42. Van Ness, column 2, last paragraph, provides motivation for using a dipstick (applicant's wand), as one of ordinary skill in the art is able to achieve "significant decrease in non-specific background signal systems." Also disclosed in column 2 is the aspect of using a multisite dipstick (wand) as such would result in increased sensitivity. Accordingly, and in the absence of convincing evidence to the contrary, the rejection is maintained.

43. At page 10, bridging to page 11 of the response of 26 June 2003 applicant asserts that Boom et al., do not teach the claimed invention and do not add anything to Van ness et al., to lead one of ordinary skill in the art to the present invention. It is also noted that applicant, at page 7 of the response also asserts:

> Boom et al. makes clear that one of ordinary skill in the art at the time of the invention would be able to determine the type of wash buffer, type of elution buffer, amount of sample and conditions necessary to practice the invention. Boom et al. does not, however, disclose the reservoir tube or the wand of the present invention. It is the technique of using a reservoir tube and wand in the method of the invention that is asserted to be novel.

As noted above, Boom et al., teach explicitly of binding nucleic acids (DNA and RNA) to silica or glass particles. Clearly, with agreement having been reached in that "Boom et al. makes clear that one of ordinary skill in the art at the time of the invention would be able to determine the

type of wash buffer, type of elution buffer, amount of sample and conditions necessary to practice the invention," as well s the use of silica particles, Boom et al., does add significantly to the rejection. Motivation for modifying the procedure of Van ness with that of Boom et al. can be found at page 495, right column, where it is stated that "[t]he procedure is inexpensive (less than $0.50 per purification for materials), and no special laboratory equipment is needed."

44. At page 11 of the response of 26 June 2003 applicant requests that attention be directed to where a seal is formed. To that end, attention is directed to Figure 1, the only figure, which shows a wand affixed to a cap, which is in turn in fixed connection with a reservoir tube. The absence of any space between the cap and the tube is construed as the cap forming a seal with the reservoir tube.

45. At page 11 applicant asserts that Wiggins does not render the claimed invention obvious as gravity and centrifugation, not agitation were used. This argument has been fully considered and has not been found persuasive as for while Wiggins dos disclose a "Centrifuge-Dependent Nucleic Acid Isolation Method" (columns 11-12), the recited method teaches explicitly of shaking the sample "vigorously" in one step and then "vortexing" the sample is yet other steps. It is further noted that Wiggins teaches explicitly of transferring the sample to different tubes (applicant's second reservoir tube, etc.). Accordingly, and in contrast to applicant's arguments, Wiggins does disclose agitation of the sample from which nucleic acids are to be isolated.

46. In view of the combined teachings of the prior art, and the explicit motivation to use microstructures on a wand, and to use fresh reservoir tubes at different steps of the method, the invention if claims 31-35, 38, 39, 63, and 65-70 remain rejected under 35 U.S.C. 103(a) as being

unpatentable over US Patent 5,514,785 (Van ness et al.) in view of Boom et al., JP 7-308184 A and US Patent 5,637,687 (Wiggins).

Conclusion

47. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

48. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

49. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

50. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

51. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
April 7, 2004